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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,643	CAYOUETTE ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *09 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60, 98, 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, and 218-222 are* is/are rejected.

7)☒ Claim(s) *60,98,175,180,185,190,196,198,202,204,212,213 and 218-222* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4-6-05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0406*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1, 27, 33, 40, 45, 48, 57, 60, 98, 100, 106, 116, 126, 131, 141, 173-175, 180, 185, 190, 196, 198, 202, 204-206, 212-214, and 218-222.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 1,27,33,40,45,48,57,100,106,116,126,131,141,173,174,205,206 and 214.

DETAILED ACTION

Applicants' election with traverse of Invention III, SEQ ID NO: 41/42, in their response of June 9, 2008, is acknowledged. The elected invention is directed to the polypeptide of SEQ ID NO: 42 and variants thereof.

Applicants' traversal is based on the argument that, as amended, all pending claims share a novel inventive concept based on the genus of polypeptides, as exemplified by SEQ ID NO: 42; see PCT rule 13.1 and 13.2 as well as MPEP 1893.03(d). This argument is not found to be persuasive. As explained in the restriction requirement of January 7, 2008, the technical feature linking the claims is that they all relate to proteases. However, said technical feature is not a special technical feature because proteases were well-known in the art. Note that MPEP 1893.03(d) states that a special technical feature is a contribution that the invention makes "as a whole" over the prior art. The requirement is still deemed proper and is therefore made FINAL.

It is acknowledged that Claims 1, 27, 33, 45, 48, and 60 have been amended. Claims 1, 27, 33, 40, 45, 48, 57, 60, 98, 100, 106, 116, 126, 131, 141, 173-175, 180, 185, 190, 196, 198, 202, 204-206, 212-214, and 218-222 are pending. Claims 1, 27, 33, 40, 45, 48, 57, 100, 106, 116, 126, 131, 141, 173, 174, 205, 206, and 214 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 60, 98, 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, and 218-222 are hereby examined.

Priority

The priority date granted for the instant invention is May 16, 2003, the filing date of US 60/471,423, which disclosed the elected invention.

Abstract

The abstract is objected to because it appears to be too long.

MPEP 608.01(b) states

> The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

Specification-Objections

The specification is objected to for the following reasons.

Table 2 and 3, pgs 119-120, are improperly formatted, with Table 3 having Table 2 inserted in the middle. For purposes of examination, Tables 2 and 3 from US 60/471,423 is used.

Claims-Objections

Claims 60, 98, 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, 218-222 are objected to for reciting non-elected subject matter.

Claims 60(ii), 190, 212, 213, 218, and 219 are objected to for the phrase "sequence as set forth in claim…". No sequences are set forth in the claims. It is suggested that said phrase be amended to "polypeptide [polynucleotide] of claim…".

Claims 212 and 220 are objected to for "ahs", which should be "has".

Claim 219 is objected to for "Clostridium botulinum toxin, a Ricin toxin", which should be "Clostridium botulinum toxin, or a Ricin toxin".

Claim 222 is objected to for "wound bed preparation, to treat….", which should be "wound bed preparation, or to treat….".

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 222 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 60, 98, 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, and 218-222 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

For Claim 60, the phrase "having at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%,

94%, 95%, 96%, 97%, 98%, 99% or more, or has 100% sequence identity to…SEQ ID NO: 42" renders the claim indefinite. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). In the present instance, the claims recite the broad recitation of "at least 70% identity", and the claims also recite "at least 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more, or has 100%", which are the narrower statements of the range/limitation. The skilled artisan would not know the metes and bounds of the recited invention. Claims 98, 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, and 218-222, as dependent from Claim 60, are indefinite for the same reasons.

For Claims 198 and 220-222, the phrase "a polypeptide having protease activity as set forth by claim 60" renders the claims indefinite. It is unclear whether said phrase means (A) a polypeptide having the structural limitations of Claim 60(i) and having a protease activity as set forth by Claim 60(ii) or (B) a polypeptide, having any structure, and having a protease activity as set forth by Claim 60(ii). The skilled artisan would not know the metes and bounds of the recited invention. Claims 98, 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, and 218-222, as dependent from Claim 60, are indefinite for the same reason. For purposes of examination, it is assumed that said phrase means a polypeptide having the structural limitations of Claim 60(i) and having a protease activity as set forth by Claim 60(ii).

For Claim 212, the phrase "Clostridium botulinum toxin in a Ricin toxin" renders the claim indefinite. It is unclear whether said phrase means "Clostridium botulinum toxin, or a

Ricin toxin" or something else. The skilled artisan would not know the metes and bounds of the recited invention. For purposes of examination, it is assumed that said phrase means Clostridium botulinum toxin, or a Ricin toxin.

For Claims 60, 98, 175, 198, 202, 212, 219, 220, and 222, the term "optionally" renders the claims indefinite. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). In the instant claims, the term "optionally" makes it unclear whether the variables listed after said term are meant to be limitations or not. In the present instance, the claims recite the broad recitation of a fusion protein lacking the variables, and the claims also recite a fusion protein comprising the variables, which is the narrower statement of the range/limitation. The purpose of the recited variables is not clear if they are not required; such recitation simply obfuscates the intended limitations.

Claims 60, 98, 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, 218-222 are rendered indefinite for improper antecedent usage as follows.

For Claims 60(ii), 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, 218-222, the phrases "a sequence of claim ….", "a polypeptide of claim….", "a polynucleotide of claim….", and "a protease activity of claim…." should be corrected to "the sequence of claim ….", "the polypeptide of claim….", "the polynucleotide of claim….", and "the protease activity of claim….". Claim 98, as dependent from Claim 60, is indefinite for the same reason.

Claim 222 provides for the use of the protease of Claim 60, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is

intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 60, 98, 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, 218-222 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protease of SEQ ID NO: 42, does not reasonably provide enablement for any polypeptide having at least 70% identity with SEQ ID NO: 42 over at least 50 amino acid residues and having any or no activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill

of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 60, 98, 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, 218-222 are so broad as to encompass any polypeptide having at least 70% identity with SEQ ID NO: 42 over at least 50 amino acid residues and having any or no activity, and compositions thereof. The scope of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO: 42 and the nucleotide sequence of SEQ ID NO: 41.

While recombinant and mutagenesis techniques as well as some protease assays are known, it is not routine in the art to screen any polypeptide having multiple substitutions or multiple modifications for any desired activity, as encompassed by the instant claims. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to

modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claims 60, 98, 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, and 218-222 which encompasses all polypeptides having at least 70% identity with SEQ ID NO: 42 over at least 50 amino acid residues and having any or no activity, and compositions thereof. The specification does not support the broad scope of Claims 60, 98, 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, and 218-222 because the specification does not establish: (A) the desired activity for all recited polypeptides; (B) which encompassed polypeptides have the functions recited in Claims 60, 198, 202, 204, 212, 213, and 218-222; (C) regions of the protein structure which may be modified without affecting the desired activity; (D) the general tolerance of the desired activity to modification and extent of such tolerance; (E) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (F) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polypeptides with an enormous number of amino acid modifications of the polypeptide of SEQ ID NO: 42. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in

the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 60, 98, 175, 180, 185, 190, 196, 198, 202, 204, 212, 213, and 218-222 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Inventors, at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of polypeptides having at least 70% identity with SEQ ID NO: 42 over at least 50 amino acid residues and having protease, digestive aid, skin care, anti-microbial, anti-viral, anti-toxin, anti-cancer, oral care, contact lens cleaning, anti-spore, pharmaceutical, anti-biological warfare, tissue dissociation, would treating, or I.V. fixation activity. The specification teaches only that the single encompassed polypeptide, SEQ ID NO: 42, has protease activity. Moreover, the specification fails to describe any other representative polypeptides by any identifying characteristics or properties other than the functionality of having protease, digestive aid, skin care, anti-microbial, anti-viral, anti-toxin, anti-cancer, oral care, contact lens cleaning, anti-spore, pharmaceutical, anti-biological warfare, tissue dissociation, would treating, or I.V. fixation activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim 175 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter that was not described in the

specification in such a way as to reasonably convey to one skilled in the relevant art that the Inventors, at the time the application was filed, had possession of the claimed invention. Claim 175 introduces the limitation of wherein, "the protease is a non-surface-active protease or a surface-active protease". The specification fails to describe said limitation and, thus, Claim 175 is rejected under 35 U.S.C. 112, first paragraph, for introducing New Matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 60, 98, 175, 180, 212, 213, 219, and 220 are rejected under 35 U.S.C. 102(b) as being anticipated by Matsuzawa et al, 1988. Matsuzawa et al teach an isolated protein having 72% identity with SEQ ID NO: 42 over 50 amino acid residues (see enclosed alignment). Matsuzawa et al further teach an array (Fig 1), a detergent composition (pg 442, parg 8), an antimicrobial (pg 442, parg 8), a textile (Table 1, Fig 1), a disinfectant (pg 441, parg 5), an anti-oxidant composition (pg 442, parg 8), and a decontamination agent (pg 442, parg 8) comprising their protein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 185, 190, 196, 198, 202, 204, 208, 221, and 222 are rejected under 35 U.S.C. 103(a) as being unpatentable over Matsuzawa et al, 1988 in view of Chen et al, 1987, Rowan et al, 1990, Outtrup et al, 1995, or Baeck et al, 1994. The teachings of Matsuzawa et al are described above. Matsuzawa et al do not teach their protease within a food product, a dairy product, paper pulp, a pharmaceutical composition, an oral care solution, a contact lens solution, a medical dressing, or a pharmaceutical composition for treating wounds. However, the use of proteases in a food product, a dairy product, paper pulp, a pharmaceutical composition, an oral care solution, a contact lens solution, a medical dressing, or a pharmaceutical composition for treating wounds was known in the art. For example, Chen et al teach meat food and a dairy product comprising a protease, Rowan et al teach pharmaceutical compositions, including wound dressings, comprising a protease, Outtrup et al teach paper pulp comprising a protease, and Baeck et al teach contact lens and oral care solutions comprising a protease. It would have been obvious to a person of ordinary skill in the art to use the protease of Matsuzawa et al in a food product, a dairy product, paper pulp, a pharmaceutical composition, an oral care solution, a contact lens solution, a medical dressing, or a pharmaceutical composition for treating wounds. Motivation to do so derive from the teachings of Chen et al, Rowan et al, Outtrup et al, or Baeck et al, who show that proteases are useful for tenderizing meat and making cheese, treating wounds, making paper, and in cleaning solutions including contact lens and oral care solutions, respectively. The expectation of success is high, as the use of proteases in a food product, a dairy product, paper pulp, a pharmaceutical composition, an oral care solution, a contact lens solution, a medical dressing, or a pharmaceutical composition for treating wounds was known in the art. Therefore, Claims 185, 190, 196, 198, 202, 204, 208, 221, and 222 are rejected under 35

U.S.C. 103(a) as being unpatentable over Matsuzawa et al, 1988 in view of Chen et al, 1987, Rowan et al, 1990, Outtrup et al, 1995, or Baeck et al, 1994.

Allowable Subject Matter

No claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages. It is also requested that the serial number of the application and date of amendment be referenced on every page of the response.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-092834. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652